Original Article

Frontal Electroencephalogram α-Asymmetry during the Luteal Phase of the Menstrual Cycle in Women with Premenstrual Syndrome

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ABSTRACT

Background: Premenstrual dysphoric disorder (PMDD) is a severe form of premenstrual syndrome (PMS) that causes significant distress and interferes with normal functioning. **Aim:** The aim of this work was to assess the resting frontal electroencephalographic patterns in females who meet criteria for PMS and PMDD. **Subjects and Methods:** This prospective observational study was conducted on 150 female participants, of which 145 had PMS, and 45 were control women. All cases were counseled about the procedure. Furthermore, a written consent was taken from every patient. Cases were asked about their current phase of the cycle, in order to determine cycle timing. The custom PMDD interview involved asking each woman a series of questions concerning PMDD symptoms. This structured interview was created from the DSM-IV-TR criteria for PMDD. Women with PMDD were asked to complete a daily symptom rating checklist for three consecutive cycles. The ensuing methods were undertaken for each patient, including history taking, general, local and fundus examination, and routine investigations, and were submitted to resting electroencephalogram (EEG) examination during both follicular and luteal phases of the cycle. **Results:** Seventy percent of women with PMS and 75% of women with PMDD exhibited left frontal activity at rest, during the luteal phase of the cycle ($P < 0.001$). **Conclusions:** We concluded that resting luteal phase of EEG frontal asymmetry must be added to the research criteria for PMDD (DSM-IV-TR).

KEY WORDS: Electroencephalogram, premenstrual dysphoric disorder, premenstrual tension, premenstrual syndrome, Tanta University Hospital

INTRODUCTION

Symptoms consistent with premenstrual syndrome (PMS) were described by Hippocrates in 460 BC. However, modern characterization of premenstrual symptoms began with a description of premenstrual tension by Frank in 1931.[1] In 1953, Green and Dalton adopted the term "PMS" to better capture the range of symptoms that women experience during the late luteal phase of the menstrual cycle.[2]

Premenstrual syndrome is marked by a variety of emotional, physical, and behavioral symptoms that occur during the late luteal phase of the menstrual cycle, and remit shortly after menstrual bleeding begins. Premenstrual dysphoric disorder (PMDD) is a severe form of PMS that causes significant distress and interferes with normal brain functioning.[3]

Clayton stated that up to 85% of menstruating women report one or more menstrual cycle-related symptoms, 20-40% report PMS and 2-9% report PMDD.[4] Takeda *et al*., conveyed that the rates of prevalence of moderate to severe PMS and PMDD in Japanese women were 5.3% and 1.2%, respectively.[5]

The diagnostic criteria of PMS were described by American College of Obstetricians and Gynecologists.[6] PMDD diagnosis requires the presence of at least 5 of the 11 symptoms specified in the DSM-IV-TR.[7]

The causes of PMDD/PMS have not been clearly elucidated but have been suggested to include hormonal changes, serotonin dysregulation, diet, drugs, and lifestyle. Previous studies suggest that high dietary Vitamin D intake may reduce the risk. However, dietary Vitamin D intake and sunlight

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exposure and the association of Vitamin D status with PMS remain unclear.[8] Genetic factors seem to contribute to the occurrence of menstrual cycle-related symptoms as well. Seventy percent of women whose mothers had PMS also have PMS, compared with 37% of women whose mothers were not affected, although these data are collected from anecdotal accounts reported by mothers and daughters. In addition, more than 90% of monozygotic twins are concordant for PMDD, while only 44% of dizygotic twins are in concordance for PMDD.[9]

The electroencephalogram (EEG), which is entirely harmless and relatively inexpensive, is the most important investigative tool in the diagnosis and management of many neurological lesions. However, for the EEG to provide accurate assessments, it must be properly performed by experienced technologists and carefully studied and interpreted in the context of a well-described clinical setting by experienced physicians. However, even a normal EEG in an untreated patient may be useful because it may exclude some conditions which an abnormal EEG is remotely unlikely to exclude.[10,11]

The present study sought to investigate changes on the resting frontal EEG related to the menstrual cycle in women with PMS and PMDD, to see whether resting head-on EEG may serve as a marker of PMS or not.

SUBJECTS AND METHODS

This prospective observational cohort study was conducted on 35 women fulfilling the criteria for a diagnosis of PMS and/or PMS[7] plus 10 matched controls. All cases were randomly recruited from the attendants of the Department of Obstetrics and Gynecology, Tanta University Hospital. Recruitment began in March 2013 and was completed in November 2013.

Participants were to be included if they provided contact information and expressed interest in further study, if they were < 35 years old, if they possessed a body mass index between 20 and 30, if they were having a regular cycle, if they were not using drug's (particularly ovulatory induction drugs, hormonal contraception, serotonin reuptake inhibitors, and other drugs affecting central nervous system during last 6 months), if they had no neurological or psychiatric problems, if they had normal fundal examination, if they had no history of previous operation in brain or spinal cord and if they reported strong right-handedness.

All patients submitted to the study were counseled thoroughly about the procedure, including the nature, value, and hazards of the investigation and the aim of the study. After this, a written consent was obtained and signed by the patients. We did not receive any funds from any person or institution. We did not classify the patients according to their religion, culture, race or any other unrelated points Approval was obtained from the relevant authority.

Once women were included within the study, they were asked about their current phase of the cycle. PMDD was diagnosed by the daily symptoms report.[12] The report consisted of 17 common PMS symptoms, including 11 symptoms from the DSM-IV PMDD diagnostic criteria.[13] Patients rated each symptom on a five-point scale, from 0 (none) to 4 (severe). The scale provided guidance for scoring the severity of each symptom, and may be used in the office setting by primary care physicians for diagnosis and assessment of PMDD.

Electroencephalogram was recorded using (NIHON KHODEN Machine, version 0.5-71, EEG, Japan). At the start, we cleaned the scalp of the patient from oil and any debris or draft. After this cleaning, 21 sliver-chloride electrodes were applied to the head surface, and they were adherent to the scalp by using adhesive conductive paste (10-20 paste). These electrodes were applied to the scalp according to the10-20 system. For each case, EEG was done twice. First, it was done on the 7th day throughout the cycle (follicular phase) and secondly, it was done on the 21st day of the cycle (luteal phase).

Statistical analysis of data was performed by the IBM SPSS (Presidion, formerly SPSS Ireland) statistics program version 20 (IBM corporation USA). Categorical variables were compared using the chi square while the numerical variables were tested using the Z-test. The value of $P < 0.05$ was taken as significant.

RESULTS

In the existent investigation, none of the 45 control cases exhibited any EEG irregularity during both follicular and luteal phases of the menstrual cycle. Likewise, all patients with either PMS or PMDD did not reveal any resting frontal EEG difference during the proliferative phase of the menstrual cycle.

Among the 105 patients fulfilling the criteria of PMS, 12 patients met the criteria of PMDD (11.43%). The EEG frontal asymmetry was found in 66 cases (70.97%) with PMS and in 9 cases (75.00%) with PMDD ($P<0.001$).

The clinical characteristics of the cases are portrayed in Table 1. From this table, it is evident that the incidence of dysmenorrhea and positive family history of PMS were significantly higher among PMS patients, in comparison with the controls.

The psychiatric symptoms of patients are shown in Table 2. Exploration of this table reveals that the most common symptoms were depressed mood (94.3%), anxiety and tension (85.7%), lethargy (68.6%), mood swings (54.3%), change in appetite (54.3%), and insomnia (54.3%).

Table 3 illustrates the association between PMS and dietary pattern among patients involved in the current investigation.

It reveals that there is statistically significant difference between the studied groups as regard depressed, sad, anxious, tense, "excited up" or on edge, mood swings/ sensitive to rejection [Figure 1]. As regards, being overwhelmed, unable to cope, breast tenderness, breast swelling, bloated sensation, weight gain, headache, joint or muscle pain, or other physical symptoms. There was no statistical significant difference between the studied groups as regards lethargy, tiredness, easy fatigability, increased appetite or food cravings, and interference in relationships with others.

Table 1: Clinical characteristics of study subjects

Variables	With PMS/ PMDD (105)	Control cases (45) (without PMS/PMDD)	*P*
Present age (in years)	21.2 (1.9)	21.6 (1.8)	0.40
Age at menarche (in years)	13.2 (1.1)	13.1 (1.0)	0.50
Number of bleeding days	5.4 (1.9)	4.7 (1.4)	0.01
Length of cycle (in days)	24.7 (9.6)	22.2 (11.3)	0.90
Family history of PMS (%)			
Yes	99 (94.29)	27 (60)	*Z*=5.249
No	6 (5.71)	18 (40)	*P*<0.001

PMS – Premenstrual syndrome; PMDD – Premenstrual dysphoric disorder

Table 2: The frequencies of neurological symptoms in subjects with PMS/PMDD

Symptom	Number	Percentage
Depressed mood	99	94.3
Anxiety	90	85.7
Lethargy	72	68.6
Mood swings	57	54.3
Insomnia or sleeping too much	57	54.3
Change in appetite, overeating	57	54.3
Anger or irritability	57	54.3
Subjective poor concentration	48	45.7
Decreased interest in usual activities	46	43.8
Feeling overwhelmed or out of control	15	14.3

PMS – Premenstrual syndrome; PMDD – Premenstrual dysphoric disorder

Table 3: Association between PMS and dietary pattern among patients

Dietary pattern	Percentage	χ^2	*P*
Sweet food			
0-2/day	62.9	1.325	0.30
>3/day	77.1		
Fast food mainly	85.7	-	-
Homemade food mainly	74.2	-	-
Vegetables and fruits			
0-1/day	77.1	3.241	0.02
>2/day	88.5		
Coffee			
1-6/week	85.7	1.635	0.20
>7 weeks	94.2		
Tea			
1-6/week	80	2.412	0.10
>7/week	88.5		

PMS – Premenstrual syndrome

DISCUSSION

Premenstrual dysphoric disorder age of onset is, usually, in early adulthood. However, correct diagnosis and treatment are often delayed after the age of 30 years.[14]

The DSM-IV diagnostic research criteria for PMDD are listed in Table 4.[13] In order to meet these criteria, a woman must suffer from a host of luteal phase symptoms and then experience a symptom-free period.

In the current study, we discovered that the mean age of patients with PMS/PMDD was 21.2 (1.9). This agrees with the results of Steiner, who reported that the average age of onset is around 26 years of age.[15] In addition, Payne *et al.*, stated the mean age of cases with PMS/PMDD as 18.3 years.[15]

In the contemporary study, we discovered that the prevalence of PMDD was 11.43% among cases that met DSM-IV-TR criteria. Wittchen *et al*., in 2002, reported a prevalence of 6% in reproductive-aged women (ages 14-24). The difference between these results and ours may be attributed to the difference in inclusion criteria of the age.[16]

The present research has shown that 94.29% of females with PMS/PMDD had a positive family history of this syndrome. Genetic factors seem to contribute to the occurrence of menstrual cycle-related symptoms as well. Seventy percent of women whose mothers had PMS also have PMS, compared with 37% of women whose mothers were not affected,

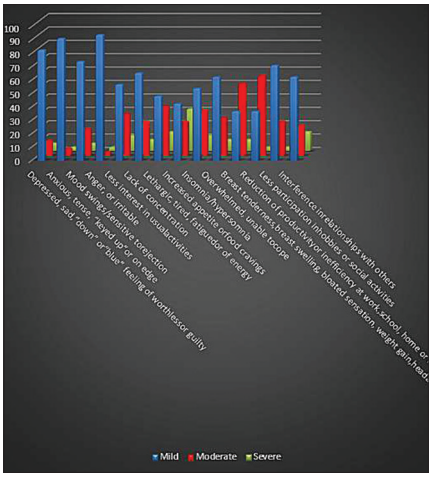

Figure 1: Premenstrual symptoms in premenstrual syndrome/ premenstrual dysphoric disorder patients, according to the severity

Table 4: Diagnostic Research Criteria for Premenstrual Dysphoric Disorder

A. In most menstrual cycles in the past year, 5 or more of the following symptoms were present for most of the time during the last week of the luteal phase, began to remit within a few days after onset of the follicular phase, and were absent during the post-menses week, with at least 1 of the symptoms being either 1, 2, 3 or 4
1. Markedly depressed mood, hopelessness, or self-deprecating thoughts
2. Marked anxiety, tension, feelings of being keyed up or on edge
3. Marked affective liability
4. Persistent and marked anger or irritability of increased interpersonal conflicts
5. Decreased interests in usual activities (e.g. Work, school, friends, hobbies)
6. Subjective sense of difficulty in concentrating
7. Lethargy, easy fatigability, or marked lack of energy
8. Marked change in appetite, overeating, or specific food craving
9. Hypersomnia or insomnia
10. A subjective sense of being overwhelmed or out of control
11. Other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of bloating, weight gain

B. Marked impairment in social or occupational function (e.g. avoidance of social activities, decreased reproductivity at work)

C. The disturbance is not an exacerbation of other symptoms of another disorder

D. Criteria A, B and C must be confirmed by prospective daily ratings during at least 2 consecutive symptomatic cycles

although these data are collected from anecdotal accounts reported by mothers and daughters. In addition, more than 90% of monozygotic twins are concordant for PMDD, whereas only 44% of dizygotic twins are in concordance for PMDD.[9]

Thirty to seventy-six percent of women diagnosed with PMDD have a lifetime history of depression[17] compared with 15% of women of a similar age without PMDD. A family history of depression is common in women diagnosed with PMS.[9] There is significant co-morbidity between depression and PMDD. Despite this relationship, many patients with PMDD do not have depressive symptoms; therefore, PMDD should not be considered as simply a variant of depressive disorder.[18] These results go along with our findings that 94.29% of our patients with PMS/PMDD had a depressed mood.

In this respect, we should refer to the work of Accortt,[19] who stated that PMDD is classified as a depressive disorder and that perhaps, the most difficult differential diagnosis for clinicians to make is to distinguish between PMDD and major depressive disorder. They are a standard comorbid disorder, and/or there is premenstrual exacerbation of major depressive symptoms.[19]

Davidson proposed that the hemispheric asymmetry in prefrontal activation, as measured by an electroencephalographic power in the alpha band, is related to reactivity to affectively valenced stimuli. Davidson has proposed further that asymmetry is a stable trait, and that left frontal hypoactivation is a stable marker of vulnerability to depression.[20]

Gotlib discovered that frontal EEG asymmetry was unrelated to mood reactivity and cognitive functioning. Studies assessing resting electroencephalographic activity revealed that relatively less left than right frontal brain activity characterizes depressed individuals, both when symptomatic, as well as when euthymic.[21] Such data raise the possibility that resting frontal EEG asymmetry will tap a diathesis toward risk for depression or other emotion-related psychopathology.[21]

Over 70 published studies have now examined the relationship between emotion or emotion-related constructs and asymmetries in EEG activity over the frontal cortex. A review of these studies suggests that asymmetries in frontal EEG activity (including resting levels of activity as well as state-related activation) are ubiquitous and involved in both trait predispositions to respond to emotional stimuli and changes in the emotional state.[22] Coan and Allen, in 2004,[23] suggested that frontal EEG asymmetry appears to serve as (1) An individual difference variable related to emotional responding and emotional disorders, and (2) a state-dependent concomitant of emotional responding.

The present study results revealed that in all patients with either PMS or PMDD, EEG did not reveal any resting frontal difference during the proliferative phase of the menstrual cycle. On the other hand, 12 out of the 105 patients fulfilling the criteria of PMS exhibited the criteria of PMDD (11.43%). The EEG frontal asymmetry was found in 66 cases (70.97%) with PMS, and in 9 cases (75.00%) with PMDD ($P < 0.001$).

Finally, based upon results, it could be hypothesized that resting luteal phase EEG frontal asymmetry must be added to the research criteria for PMDD (DSM-IV-TR).

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